Molecular Structure of Veratrobasine

Sir:

We report an X-ray diffraction determination of the structure and stereochemistry, except for absolute configuration, of the steroid alkaloid veratrobasine ($C_{27}H_{41}O_3N$), which is present in the perennial *Veratrum album* (the European hellebore).[1] This determination establishes the correct empirical formula, proves that an N-methyl group is *not* present, and helps to elucidate the relationships of veratrobasine to the other *Veratrum* alkaloids, particularly to jervine.

The space group is $P2_12_12_1$, and there are four molecules in a unit cell of dimensions $a = 8.385$, $b = 15.773$, and $c = 18.037$ Å. Of the 3105 unique diffraction maxima, within reciprocal space accessible to Cu radiation, 3077 were recorded by the multiple-film Weissenberg method, and visual estimates were obtainable for all but 378 of these.[2] In the course of several years of investigation, a number of crystallographic methods failed to provide a solution of this structure.[2] The structure was finally solved by the symbolic addition procedure of Karle and Karle,[3] in which phases were assigned to three reflections to fix the origin, phases of six other structure invariants were obtained from the Σ_1 formula,[4] and two phases were assigned symbols of unknown values, one of which determined the enantiomorph. The 52 phases determined by symbolic addition were used as input to the tangent formula[3] by which phases were assigned to 636 reflections having normalized structure factors, E, greater than 1.1. Convergence was achieved in 14 min on an IBM 7094 computer with the use of a program written in this laboratory (by G. N. R.). Refinement, first with the use of the tangent formula[5] and then by Fourier and least-squares methods, has reached a value of 0.11 for the R factor ($R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$) after inclusion of all hydrogen atoms and assumption of isotropic thermal parameters. At this stage of refinement, bond distances and angles are near expected values: for example, the average $C(sp^3)$–$C(sp^3)$ distance is 1.53 ± 0.02 Å.

The identity of the N and O atoms was established with certainty by refinements in which all non-H atoms were assumed to be carbon, and the behavior of atom multipliers and apparent thermal parameters was examined. Difference electron density maps and interatomic distances were also examined.

The structure (Figure 1) has a bonding skeleton like that of jervine except that veratrobasine has a hydroxyl group at C_{11} whereas jervine has a keto group. This hydroxyl group is strongly indicated by the bond angles about C_{11} and by the C–O distance of 1.46 Å. Both veratrobasine and jervine contain the highly unusual C-nor-D-homo steroid ring system. It remains to be shown whether the stereochemistry of the two molecules is identical at corresponding asymmetric centers. Although the absolute configuration was not established in this study, we have chosen for the A and B rings the configuration which occurs in normal steroids, such as cholesterol.

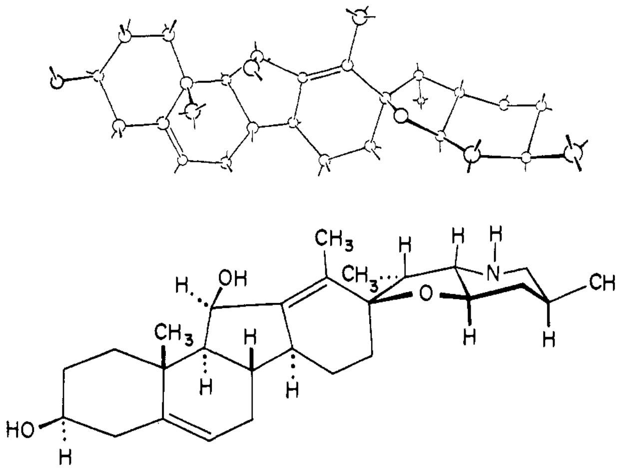

Figure 1. (a) Stereochemical drawing from a model of the veratrobasine moleculcule (upper); (b) conventional chemical representation of the stereochemistry of veratrobasine (lower).

An apparent difficulty in measurements of the molecular weight has led to reports of the incorrect empirical formula, $C_{24}H_{37}O_3N$.[1,6,7] Hitherto, the veratrobasine molecule has been believed[1,6] to contain an N-methyl group as a tertiary amine, which is at variance with the monobenzoylation reaction.[6] Our structure determination shows that the N-methyl group is not present and thereby provides a basis for the explanation of some of the more puzzling chemical results.[6]

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[1] A. Stoll and E. Seebeck, *J. Am. Chem. Soc.*, **74**, 4728 (1952).

[2] R. Lewin, Ph.D. Thesis, Harvard University, 1964. The primary X-ray data are available in this thesis.

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[4] J. Karle and H. Hauptman, *ibid.*, **9**, 635 (1956).

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A Novel Bidentate π-Bonding Ligand Derived from 1,2-Dicarba-*closo*-dodecaborane(12)

Sir:

A variety of transition metal complexes with eleven-particle icosahedral carborane fragments have been reported.[1] We wish to report a complex containing

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[1] (a) M. F. Hawthorne, D. C. Young, T. D. Andrews, D. V. Howe, R. L. Pilling, A. D. Pitts, M. Reintjes, L. F. Warren, Jr., and P. A. Wegner, *J. Am. Chem. Soc.*, **90**, 879 (1968); (b) D. E. Hyatt, J. L. Little, J. T. Moran, F. R. Scholer, and L. J. Todd, *ibid.*, **89**, 3342 (1967); (c) L. F. Warren, Jr., and M. F. Hawthorne, *ibid.*, **89**, 470 (1967); (d) W. H. Knoth, *ibid.*, **89**, 3342 (1967); (e) P. A. Wegner and M. F. Hawthorne, *Chem. Commun.*, 861 (1966); (f) M. F. Hawthorne and T. D. Andrews, *ibid.*, 443 (1965); (g) A. Zalkin, T. E. Hopkins, and

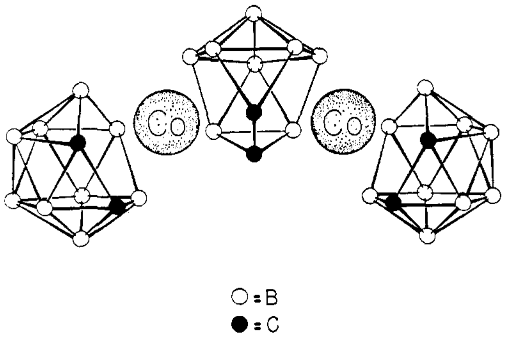

Figure 1. Skeletal structure of $[(C_2B_9H_{11})Co(C_2B_8H_{10})Co(C_2B_9H_{11})]^{2-}$.

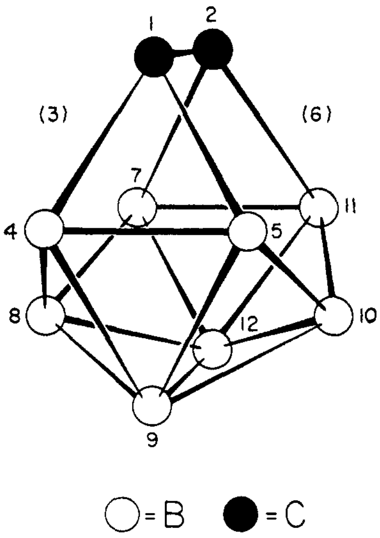

Figure 2. Skeletal structure of the (3,6)-1,2-dicarbacanastide ion.

the first example of a bidentate π-bonding ligand which is derived from a ten-particle icosahedral fragment.

We have used the reaction of $1,2\text{-}B_9C_2H_{11}^{2-}$ with transition metal hydroxides (formed *in situ* from the chlorides in hot aqueous base) as a convenient preparation of the $(B_9C_2H_{11})_2M$ systems.[1a,c] Precipitation of the orange $Rb^+[(B_9C_2H_{11})_2Co^{III}]^-$ from an aqueous solution of the ether-soluble products of such a reaction leaves a red solution, from which we have isolated in low yield (1%) a new ion (I) as the cesium salt. Yields of 15% may be obtained by treating preformed $K^+[(B_9C_2H_{11})_2Co^{III}]^-$ with 30% aqueous NaOH and excess $CoCl_2$ for several hours at 100°. The iron and nickel complexes do not give similar reactions under these conditions.

A single-crystal X-ray diffraction study[2] has now confirmed that the compound has the structure presented in Figure 1. For the novel central ligand (Figure 2) we propose the root name "canastide," from the Spanish noun for basket. Thus, the name of the central ion would be the (3,6)-1,2-dicarbacanastide(−4) ion, and that of compound I would be bis-π-[(3)-1,2-dicarbollylcobalt]-π-(3,6)-1,2-dicarbacanastide(−2) ion. *Anal.* Calcd for $[C_6H_{32}B_{26}Co_2]Cs_2 \cdot H_2O$: C, 9.16; H, 4.35; B, 35.73; Co, 14.92. Found: C, 9.60; H, 4.34; B, 36.47; Co, 14.63. The 60-Mc/sec ^1H nmr spectrum in acetone solution contained resonances at δ 3.8 (broad, 4 H) and 4.63 (broad, 2 H). These resonances can be assigned to the protons on the carbon atoms of the two outer and central ligands, respectively. The protons attached to the boron atoms gave resonances too broad to be observed. The 32-Mc/sec ^{11}B nmr shows a doublet at δ −21 (ppm from $BF_3 \cdot OEt_2$) of area 2, and an envelope from δ −6 to +26 of area 26 resembling the spectrum of $(B_9C_2H_{11})_2Co^-$. The infrared spectrum (Nujol mull) contained bands at 1595, 3580, and 3450 cm^{-1} due to a water of crystallization, as well as carborane CH (3000 cm^{-1}) and BH (2500 cm^{-1}) bands. Electronic spectra of the $(CH_3)_4N^+$ salt in acetonitrile revealed λ_{max} (ε) at 297 mμ (40,000) and 324 mμ (30,000) sh, and a long-wavelength end absorption, 800 mμ (160). Cyclic voltammetry in acetonitrile showed two reversible couples with half-wave potentials +0.95 and −1.50 V (*vs.* sce).

Presumably, a boron of one of the cages of the $(B_9C_2H_{11})_2Co^-$ complex is removed by the strong base, and the open face so formed then complexes with another cobalt atom and a $B_9C_2H_{11}^{2-}$ ion. The $B_9C_2H_{11}^{2-}$ ion must arise from the dissociation or degradation of the starting material. To confirm the availability of the $B_9C_2H_{11}^{2-}$ ion in solution, $(B_9C_2H_{11})_2Co^-$ was treated under the same conditions with nickelous chloride. Benzene was added to the cooled reaction mixture, and air was bubbled through the whole for several hours. A low yield (1–2%) of $(B_9C_2H_{11})_2Ni$,[1c] identified by infrared spectroscopy and thin layer chromatography R_f values, could be obtained from the benzene solution. The solution remaining contained a variety of products, among them, presumably, a complex similar to I, but containing one nickel and one cobalt atom, which has not been isolated.

The existence of the (3,6)-1,2-dicarbacanastide ion suggests the possible existence of a large family of new metal complexes, some of which may contain cyclic ligand–metal arrays and highly delocalized bonding electrons. An intensive investigation of this chemistry is in progress.

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A Simple Trimerization of 2,3-Butanedione Yielding a Selective Reagent for the Modification of Arginine in Proteins

Sir:

Selective modification of amino acid side chains in proteins constitutes an important avenue for correlation